Clostridium difficile-Associated Diseases (CDAD)

Manitoba

Communicable Disease Control Unit

Definitions

Case Definition: A diagnosis of CDAD applies to a person with:

- Acute onset of diarrhea (loose stool). Loose stool is defined as that which takes the shape of the container that holds it

  And

- Laboratory confirmation (positive *Clostridium difficile* toxin, culture with evidence of toxin production or histological/pathological diagnosis of CDAD)

  Or

- Diagnosis of typical pseudo-membranes on endoscopy

  Or

- Diagnosis of toxic megacolon supported by diagnostic imaging (1-3).

Patient: For the purposes of this document "patient" refers to patients, residents, clients.

Nosocomial Case (current facility):

- Patient's initial symptoms occur greater than 48 hours post-admission to a health care facility.

  Or

- A patient, who has been discharged from the current health care facility within the preceding four weeks, who develops an onset of CDAD which requires readmission to the same health care facility.

Nosocomial Case (imported from different facility):

- Patient's initial signs of diarrhea occur within 48 hours post-admission to a health care facility, or attendance in out-patient.

  And

- The patient has been discharged from or has been in ambulatory care in a different health care facility in the preceding four weeks (7, 8).

Community Acquired Case:

- Patient does not meet either Nosocomial Case definition.

Recurrent Case:

- Individuals who have a second confirmed episode of CDAD between the end of treatment and eight weeks from the end of treatment of the first episode (5, 6), are classified as recurrent cases.
- If the second episode is greater than eight weeks from the end of treatment date, it is no longer considered a recurrence. It is classified as a *new case*.
- If two *C. difficile* toxin positive specimens are separated by under two weeks, the second specimen is described as an additional test result of the original episode, and not counted as a recurrence.

Laboratory Diagnostic Test Criteria and Diagnosis

Unpreserved stool specimens should be sent to a clinical/medical laboratory when CDAD is suspected. Diagnosis of CDAD can be made by detecting Toxin A and/or B by using the Enzyme Immuno Assay (EIA) or Immunocard methods, or by detecting Toxin B in the Cytopathic Effect (CPE) assay. A diagnosis of CDAD can also be made by successful culture of *C. difficile*, followed by a demonstration that the isolate is toxigenic. In most cases, toxin testing of a single stool specimen effectively establishes the diagnosis. **The unpreserved specimen should be sent as soon as possible after suspected clinical diagnosis.** A maximum of two stool samples per diarrhea episode (collected on separate days) will be tested. If clinically CDAD is highly suspected but the diagnostic tests are negative, culture may be warranted to determine if an unusual *C. difficile* strain is present (e.g., genetic alteration of the toxin genes).

When *C. difficile* immunoassay tests (for species identification and presence of toxin) produce equivocal results, further testing (tissue culture confirmation) is required. The currently used Triage® test in combination with CPE testing to resolve discordants has a sensitivity of 93% and a specificity of 89% (9). The test has been evaluated and confirmed to be reliable for detection of *C. difficile* toxin in human stool when used correctly (9).

Note: Liquid or loose stool sample which takes the shape of the container more than 1/3 full (25mL) without preservatives must be submitted to ensure a reliable laboratory result. Formed stool is not an appropriate specimen and will not be tested for *C. difficile* by most laboratories. If transport is more than two hours, the sample must be refrigerated.

Reporting Requirements

- All positive laboratory tests for *C. difficile* toxin are reportable by the laboratory to the Director, Communicable Diseases Control Unit, Manitoba Health.
- CDAD diagnoses based on endoscopy and other imaging techniques are reportable by the ordering practitioner to the Director, Communicable Diseases Control, Manitoba Health.
- Infection Prevention and Control Practitioners or designated individuals in health care facilities are required to complete the Manitoba Health Communicable Diseases Control Unit Investigation Form for CDAD for each confirmed case of CDAD infection diagnosed at their facility. Outcomes must be reviewed at **30 days post-diagnosis** and the investigation form returned to the Communicable Diseases Control Unit of Manitoba Health.
- Manitoba Health, Public Health Branch will consider enhanced surveillance on community acquired infections.
- Outbreaks require individuals responsible for infection control and infectious disease to provide notice to the Communicable Diseases Control Unit, Public Health Branch, Manitoba Health.

Clinical Presentation

Toxigenic *Clostridium difficile* may cause self-limiting or severe diarrhea, progressing to pseudomembranous colitis syndrome, which may result in many (mucousy, foul smelling) stools per day. Accompanying symptoms may include fever, lethargy, abdominal pain, bloating or cramping, as well as hypotension and dehydration. Infrequently, *C. difficile* colitis also presents without diarrhea as an acute abdominal syndrome or toxic megacolon. Leukocytosis is common. In addition, there is often a history of antibiotic use within the previous 10 weeks (4, 7, 8).

Etiology

Clostridium difficile is an opportunistic, gram positive, spore-forming anaerobic bacillus. Pathogenicity is usually associated with the production of two toxins, A (enterotoxin) and B (cytotoxin). The genes for these toxins are found in the Pathogenicity Locus (PaLoc) on the chromosome of some strains of *C. difficile*. In addition, there is also evidence that another toxin called binary toxin is produced by some strains but its role in CDAD is currently unknown. Non-toxigenic strains of *C. difficile* have not been associated with CDAD. When the normal intestinal flora is disrupted by use of antibiotics, colonization resistance is lost and organisms such as *C. difficile* may cause disease in patients rendered susceptible. The actively replicating (vegetative) organism produces toxin and this leads to CDAD. The spore form does not produce toxin but if allowed to convert to the vegetative form, it can cause CDAD.

Epidemiology

Reservoir and Source: The reservoir is mainly humans; however, spores are also present in soil and water. The source of *C. difficile* may be either endogenous (colonized patients' own flora) or exogenous, such as hospital environment and equipment (commodes, bedrails, and bedpans) that have been contaminated with stool. In healthy adults, intestinal carriage rate of toxigenic

C. difficile is approximately three to eight per cent. Asymptomatic colonization rate of hospital inpatients is reported to be higher, at around 20%. In healthy neonates colonization rate is reported to be as high as 70%.

Transmission: Through fecal-oral transmission, direct contact or indirect contact transmission via hands or items contaminated with stool from symptomatic and/or asymptomatic (colonized) patients.

Occurrence:

World wide: Due to frequent use of various antibiotics, CDAD has become a leading cause (20-45%) of all hospital-acquired diarrhea. The reported frequency among acute care hospitalized patients ranges from one to more than 25 per 1,000 discharges. Local prevalence rates may vary depending on antibiotic prescribing patterns, endemic strains, and criteria used to define antibiotic associated diarrhea.

Manitoba: CDAD became reportable April 18, 2005. Preliminary results show between 100 and 130 cases per month. The disease may demonstrate a seasonal trend.

Incubation Period: The onset of clinical disease is typically 5-10 days after initiation of antimicrobial treatment; however, diarrhea may develop as early as the first day or as late as 10 weeks after cessation of antimicrobial therapy.

Susceptibility and Resistance: The main contributing factor of CDAD is the type and duration of previous antibiotic therapy. Other factors associated with CDAD are advanced age, severity of underlying illness, length of hospital stay, the usage of agents that alter normal intestinal motility, tube feeding, and cancer chemotherapy.

Period of Communicability: Period of communicability is not well defined because asymptomatic patients may be colonized with the bacteria and patients who have been successfully treated may still have organisms and spores in their stools.

Key Investigations

- Toxin positive reports sent by laboratories to Manitoba Health, Public Health Branch will be included in ongoing *C. difficile* surveillance.
- CDAD diagnoses based on endoscopy and other imaging techniques will be included in ongoing *C. difficile* surveillance.
- Infection Prevention and Control Practitioners in health care facilities are required to complete the Manitoba Health Communicable Diseases Control Unit Investigation Form for CDAD for each confirmed case of CDAD infection diagnosed at their facility.
- Community cases reported to Manitoba Health, Public Health Branch will be monitored for *C. difficile* surveillance.

Management of Cases

Treatment:

- Discontinue all current antibiotic therapy, if possible.
- Do not use antidiarrheal agents until CDAD has been excluded.

Treatment recommendations:

- First episode, treat with Metronidazole 500mg P.O. t.i.d. for 10-14 days.
- First relapse, treat with Metronidazole 500mg P.O. t.i.d. for at least 14 days.
- Second relapse, treat with Vancomycin 125mg P.O. q.i.d. for 10-14 days.
- Third relapse, consult with infectious diseases/ gastroenterology.
- Complicated cases or excessive relapses should be treated based on recommendations following consultation of infectious disease specialists.

Note: Test of cure is not indicated. If patient is asymptomatic, further testing for *C. difficile* is not indicated. Resistance of *C. difficile* to metronidazole or vancomycin is rare and recurrence of disease is usually not due to antibiotic resistance to these medications.

Infection Control Practices

Health Care Facilities: Symptomatic individuals in health care facilities must be placed on Routine Practices in addition to Contact Precautions, as recommended by the Public Health Agency of Canada (PHAC) Guidelines (See **Additional Resources**). Contact Precautions should be maintained until 48 hours after diarrhea has resolved (see **CDAD Infection Control Guidelines**).

Community Settings: Manitoba Health's Infection Control Guidelines for Health Care Workers in the Community must be followed when providing care to symptomatic individuals in the community (See **Additional Resources**).

Management of Contacts

Contact investigation is not required.

Management of Outbreaks

- In health care facilities, when outbreaks of CDAD occur, further investigation and epidemiological testing should be carried out in consultation with those responsible for Infection Prevention and Control and Infectious Disease.
- Facility outbreaks must be reported to the Communicable Diseases Control Unit of Manitoba Health, Public Health Branch.

Preventative Measures:

- Public education in personal hygiene, especially hand hygiene (see **Routine Practices and Additional Precautions for Preventing the Transmission of Infection in Health Care, PHAC document**).
- Promote responsible stewardship of community and institutional use of antimicrobials.

Transfer Between Facilities: The diagnosis of CDAD does not preclude transferring patients between facilities or movement to and from Long Term Care Facilities. Patients with CDAD should have their status noted on their health record. Patients with CDAD should have this clearly documented on the Regional Health Authorities of Manitoba Transfer Referral Form. Negative culture/toxin results are not required for transfer. Agencies responsible for transferring patients with positive CDAD diagnoses require notification that Contact Precautions should be used during the transfer if the patient is considered infectious.

Additional Resources

1. Routine Practices and Additional Precautions for Preventing the Transmission of Infection in Health Care, Public Health Agency of Canada, Laboratory Centre for Disease Control. July 1999. http://www.phac-aspc.cc.ca/new_e.html
2. Infection Control Guidelines for Health Care Workers in the Community, Manitoba Health. January 2005. http://www.gov.mb.ca/health/publichealth/cdc
3. Infection Control Guidelines for *Clostridium difficile*, Manitoba Health. February 2006. http://www.gov.mb.ca/health/publichealth/cdc

Additional Forms

- Manitoba Health CDC Unit Investigation Form for CDAD.

References

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